UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,271	12/11/2000	Mark Daly	2825.1025-002	7597

21005 7590 09/03/2002

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER	
SOUAYA, JEHANNE E	
ART UNIT	**PAPER NUMBER**
1634	11

DATE MAILED: 09/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/735,271	DALY ET AL.	
	Examiner	Art Unit	
	Jehanne Souaya	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9,10 and 12* is/are rejected.

7)☒ Claim(s) *8 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of a method for predicting the likelihood that an individual will have an IBD or Crohn's disease by determining the nucleotide present at position 218 of SEQ ID NO 1127 in Paper No. 10 is acknowledged. It is noted that the original claims were directed to assessing the genotype of an individual by determining the identity of a polymorphic site selected from 1064 different sequences. Applicants canceled those claims and inserted 6 new claims drawn to a method of predicting the likelihood that an individual will have an IBD or Crohn's disease by determining the nucleotide present at a specific position for 11 different sequences. The traversal is on the ground(s) that the 11 sequences are part of a markush group and that the MPEP states that if members of a Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the Examiner must examine all the claims. This is not found persuasive because in the previous office action, the examiner indicated that if applicant's found that the sequences were not patentably distinct, such should be shown on the record. In response, applicants have only stated that the sequences are part of a haplotype. It is noted however, that the claim is only drawn to "one or more" of 11 of the 12 polymorphisms that the specification indicates as part of a haplotype. Therefore, as the response clearly does not state that the sequences are not patentably distinct, the examiner maintains that the polymorphisms identified in the claims are each found in distinct sequences with distinct structures and functions, and are

therefore patentably distinct. With regard to the traversal regarding the search burden, the examiner further maintains that searching each of the 11 polymorphisms in the sequence databases as well as the databases of scientific journals and patents, to identify the sequences themselves, their relevance to IBD and Crohn's disease, as well as each individual polymorphism does pose a serious search burden on both the examiner and the office. With regard to applicant's assertion that the restriction should be an election of species, as stated above, each polymorphism is found in an independent and distinct sequence and the examiner stated in the previous office action that the restriction requirement was NOT an election of species (see p 2, last line of second paragraph of the previous restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

2. An action on the merits of claims 7-12, drawn to methods of predicting likelihood of IBD or Crohn's disease by determining the nucleotide present at position 218 of SEQ ID NO 1127 follows.

Claim Objections

3. Claims 8, 9, 11, and 12 are objected to because of the following informalities: the claims are dependent on rejected claims. Appropriate correction is required.

Specification

4. The disclosure is objected to because of the following informalities: .

The specification contains an embedded hyperlink and/or other form of browser-executable code, for example see p. 33. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is required.

5. The substitute specification has been entered.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 7, 9-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of predicting the likelihood that an individual will have Crohn's disease by determining the nucleotide present at position 218 of SEQ ID NO 1127, wherein the presence of a guanine at position 218 is indicative of a greater likelihood of having Crohn's disease in the individual as compared with an individual having a cytosine at position 218, or wherein the presence of a cytosine at position 218 is indicative of a reduced likelihood of having Crohn's disease in the individual as compared with an individual having a guanine at position 218, does not reasonably provide enablement for a method of predicting the likelihood that an individual will have any inflammatory bowel disease by determining the

nucleotide present at position 218 of SEQ ID NO 1127, wherein the presence of a guanine at position 218 is indicative of a greater likelihood of having any inflammatory bowel disease in the individual as compared with an individual having a cytosine at position 218, or wherein the presence of a cytosine at position 218 is indicative of a reduced likelihood of having any inflammatory bowel disease in the individual as compared with an individual having a guanine at position 218, or wherein the individual is an individual at risk for development of Crohn's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of predicting the likelihood that an individual will have *any* inflammatory bowel disease by determining the nucleotide present at position 218 of SEQ ID NO 1127, wherein the presence of a guanine at position 218 is indicative of a greater likelihood of having any inflammatory bowel disease in the individual as compared with an individual having a cytosine at position 218, or wherein the presence of a cytosine at position 218 is indicative of a reduced likelihood of having *any* inflammatory bowel disease in the individual as compared with an individual having a guanine at position 218, or wherein the individual is an individual at risk for development of Crohn's disease. The specification teaches that a haplotype consisting of 12 SNPs in an 250 kb region of chromosome 5q31-q33 was associated with 6 Crohn's Disease (CD) patients. The specification also specifically teaches that a G at position 218 of SEQ ID NO 1127 has a statistically significant association (see table 4 in the

specification) with CD. The claims, however, broadly encompass any inflammatory bowel disease, whereas the specification provides no teaching or working examples that a G at position 218 of SEQ ID NO 1127 has a statistically significant association with any inflammatory bowel disease.

An association with the claimed polymorphism and any IBD, such as UC, based on data only obtained with patients with CD is clearly unpredictable given the state of the art. Rector et al (Genes and Immunity, vol. 2, pp 323-328, October 2001, abstract included) teach that inflammatory bowel diseases (IBD), CD, and UC are complex multifactorial traits involving both environmental and genetic factors (see abstract). Rector teaches that a study of point mutations in codons 52, 54, and 57 of exon 1 of mannan-binding lectin, which plays an important role in non specific immunity, were significantly lower in frequency in UC patients when compared with CD patients. Lesage et al (American Journal of Human Genetics, vol 70, pp 845-857, 2002) teaches that CARD15/NOD2 encodes a protein involved in bacterial recognition by monocytes and that mutations in CARD15 have been associated with CD. Lesage teaches that an analysis of 3 polymorphisms which were independently associated with susceptibility to CD were not associated to UC (see abstract). Further, Over et al (European Journal of Gastroenterology and Hepatology, vol. 10, pp 827-829, 1998, abstract included) teaches that a study that tested the frequency of a point mutation in factor V (FV Leiden), which has been identified in various thromboembolic diseases, found that FV Leiden was found to be statistically more frequent in CD patients but not in UC patients (see abstract). Thus, as exemplified by the state of the art

regarding polymorphisms in genes and their association with IBD's, an association between specific polymorphisms and any IBD, such as UC, based on an association with such to CD, is unpredictable. Although polymorphisms in some genes have been linked to both CD and UC, a large number of polymorphisms are also associated to only one disease and not the other, as exemplified by the cited art. Therefore, the art does not provide the skilled artisan with a predictable correlation that polymorphisms linked to CD are also linked to any IBD, such as UC. To practice the invention as claimed, the skilled artisan would have to perform a large study of patients with different types of IBD's, such as UC, and matched controls to determine if the polymorphism claimed was associated with any IBD. Such a study would consist of mainly trial and error analysis, the outcome of which is clearly unpredictable as exemplified by the state of the art. Therefore, given the lack of guidance from the specification as to any statistical association between the claimed polymorphism and any IBD other than CD, such as UC, and the unpredictability taught in the art as to an association between polymorphisms associated with both CD and UC, for example, the skilled artisan would be required to perform undue experimentation to practice the invention as broadly as it is claimed. It is noted that claims 9 and 12 which specify that the individual is one at risk for developing CD are also not enabled by the specification for the reasons made of record above. In addition, as exemplified by the cited art, the art teaches that mutations or polymorphisms in certain genes which are linked to CD are not linked to UC. Therefore, the fact that an individual was already categorized as at risk for developing CD would not provide a predictable correlation that the individual was at risk for *any*

IBD because the art teaches that mutations in patients that actually have CD are not necessarily linked to patients with any IBD, such as UC.

Conclusion

8. Claims 8 and 11 are free of the prior art and enabled by the specification's disclosure.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
August 22, 2002